

REMARKS

Applicant respectfully requests reconsideration. Claims 1, 2, 5-8, 11, 16, 17 and 30-33 are pending in this application with claim 1 being an independent claim. No new matter has been added.

Rejections under 35 U.S.C. §112

The Examiner rejected claim 31 under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement. The Examiner has indicated that the claim contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The Examiner alleges that no support is found in the instant specification for the alpha-lactalbumin promoter.

Applicant respectfully traverses. On page 2 of the instant specification, it is taught that the promoter can be that of a milk serum protein or a casein protein. Examples of milk serum proteins, which include alpha-lactalbumin, are given, for example, on page 4 of the instant specification (See, e.g., lines 6-15). It follows that the combination of these passages give support for milk serum protein promoters, such as the alpha-lactalbumin promoter, and not just the milk serum proteins themselves. The Examiner is respectfully reminded that *in haec verba* support (i.e., literal support) is not required for the disclosure to satisfy the written description requirement, and a term can be supported in the specification through express, implicit or inherent disclosure. See MPEP 2163(I)(B) and 2163.02. Applicant maintains that the above-mentioned passages provide support for the alpha-lactalbumin promoter through express, implicit or inherent disclosure, and the rejected term, therefore, does not constitute new matter.

In addition, Applicant notes that the Examiner has the initial burden of presenting by a preponderance of evidence why a person skilled in the art would not recognize in Applicant's disclosure a description of the invention defined by the claims. Wertheim, 541 F.2d at 263, 191 USPQ at 97. Applicant maintains that the Examiner has not demonstrated by a preponderance of evidence that one of ordinary skill in the art would not have recognized that the alpha-lactalbumin promoter is described in view of the disclosure of the application as filed.

Applicant respectfully requests withdrawal of this rejection.

Claims 1, 2, 5-8, 11, 16, 17 and 30-33 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The Examiner has indicated that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant respectfully traverses. Before addressing the substance of this rejection, Applicant will address its procedural deficiency. The description as filed is presumed to be adequate, unless or until sufficient evidence or reasoning to the contrary has been presented by the Examiner to rebut the presumption. See, e.g., *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971). The Examiner, therefore, must have a reasonable basis to challenge the adequacy of the written description and has the initial burden of presenting by a preponderance of evidence why a person skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims. *Wertheim*, 541 F.2d at 263, 191 USPQ at 97. MPEP 2163.04. Applicant maintains that the Examiner has failed to present any evidence, let alone a preponderance of evidence, to demonstrate that a person skill in the art would not recognize a description of the mammalian milk protein promoters. All that is provided are the Examiner's opinions.

First, the Examiner argues that, except for the WAP promoter, the instant disclosure only provides examples of mammalian milk proteins and not promoters. As demonstrated above, this is not the case. The instant specification clearly describes promoters by specifying that the promoters can be derived from any of a number of examples of mammalian milk proteins. The genus of milk proteins can be divided into subgenera: the milk serum protein promoters (promoters of WAP, alpha-lactalbumin and beta-lactoglobulin) and the casein protein promoters (promoters of alpha, beta, kappa and gamma casein). The instant specification provides that the promoter can be that of a milk serum protein or a casein protein (See, e.g., page 2 of the instant specification). In addition, specific examples of milk serum proteins are provided and include WAP, alpha-lactalbumin and beta-lactoglobulin. (See, e.g., page 4, lines 6-15, and page 15, lines 2-10 of the instant specification). Such teachings go beyond the disclosure of only the recited proteins as argued by the Examiner. Again, *in haec verba* support is not required for the disclosure to satisfy the written description requirement, and a term can be supported in the

specification through express, implicit or inherent disclosure. See MPEP 2163(I)(B) and 2163.02. Applicant maintains that the above-mentioned passages provide support for the promoters of these proteins and is sufficient to convey to one of ordinary skill in the art that the inventors has possession of the genus of mammalian milk protein promoters.

Second, the Examiner argues that the DNA sequences of the promoters are required. The Examiner cites two cases, Fiers v. Fevel and Amgen v. Chugai to support this alleged requirement. Fiers v. Fevel and Amgen v. Chugai, however, are easily distinguishable from the facts of the instant case. The gene sequences at issue in these two cited cases were novel gene sequences having no sequence structure known in the art and defined only by their function. The sequences of mammalian milk protein promoters, however, were known in the art at the time the instant application was filed. Provided herewith are five references, which exemplify the knowledge in the art at the time the instant application was filed, and which provide the cloned genomic sequence, identify the 3' end of the 5' regulatory region, identify the characteristic 5' regulatory structures and provide a significant amount of DNA sequence for the promoter regions of five of the seven types of mammalian milk protein promoters. See Qsaba and Safaya (1984), *Similarity of the nucleotide sequences of rat α -lactalbumin and chicken lysozyme genes*, Nature, Vol. 308 (Exhibit A); Campbell and Rosen (1984), *Comparison of the whey acid protein genes of the rat and mouse*, Nucleic Acids Research, Vol. 12, No. 22 (Exhibit B); Yu-Lee et al. (1986), *Evolution of the casein multigene family: conserved sequences in the 5' flanking and exon regions*, Nucleic Acids Research, Vol. 14, No. 4 (Exhibit C); Jones et al. (1985), *The Rat Casein Multigene Family: Fine Structure and Evolution of the β -Casein Gene*, The Journal of Biological Chemistry, Vol. 260, No. 11 (Exhibit D); Yu-Lee and Rosen (1983), *The Rat Casein Multigene Family: I. Fine Structure of the γ -Casein Gene*, The Journal of Biological Chemistry, Vol. 258, No. 17 (Exhibit E). Promoter regions for at least two of three types of milk serum proteins were known as were at least three of four types of caseins. The Examiner is respectfully reminded that information which is well known in the art need not be described in detail in the specification. See, e.g., Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1379-80, 231 USPQ 81, 90 (Fed. Cir. 1986) and MPEP 2163.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species. MPEP 2163.05. The description of one or more species is representative, and adequately describes the genus, when the evidence indicates ordinary artisans would predict the operability of any of the species of mammalian milk protein promoters based on the representative species. In re Curtis, 354 F.3d 1347, 1358, 69 USPQ2d 1274, 1282 (Fed. Cir. 2004). As demonstrated above, the instant specification provides a description of a number of species of the small genus of mammalian milk protein promoters, a large proportion of which was well-characterized and defined in the art at the time of the filing of the instant application. In addition, the operability of any of the species of mammalian milk protein promoters would have been predicted by one of ordinary skill in the art at the time the instant application was filed based on the disclosure provided.

At the time the invention was made, many genes encoding milk proteins had been cloned and transcriptional regulatory sequences involved in their expression identified and at least partially characterized, and it was generally understood that milk protein genes might share one or more regulatory elements conferring mammary specific and hormone controlled expression. See Paragraph 6 of the Third Declaration Under 37 CFR 1.132 of Katherine Gordon¹. Additionally, the milk proteins coordinately expressed in lactating mammary epithelia were presumed to share similar regulatory mechanisms for expression and one skilled in the art, at the time the invention was made, and in light of the disclosure in the application, would have reasonably expected that transcriptional regulatory sequences derived from other members of the class of milk serum proteins would function within the same or similar manner as the WAP regulatory sequences. See Paragraph 7 of Ibid. Therefore, the disclosure of the species provided in the instant specification adequately describes the genus, as the evidence indicates ordinary artisans would have predicted the operability of any of the species of mammalian milk protein promoters based on Applicant's teachings.

Further, Applicant is also providing herewith three post-filing references that demonstrate that due to Applicant's invention, those of ordinary skill in the art were able to successfully

¹ To ensure the record is complete for a potential appeal, Applicant is providing herewith a copy of this (Exhibit F) as well as all other declarations that were filed in Application Serial No. 07/938,322, now U.S. Patent No. 7,045,676 (Exhibits G-J).

express genes of interest using promoters of casein proteins and all of the above-mentioned mammalian milk serum proteins in a number of species (e.g., mouse, goat, pig, sheep, rabbit and cattle). See Maga and Murray (1995), *Mammary Gland Expression of Transgenes and the Potential for Altering the Properties of Milk*, Bio/Technology, Vol. 13 (Exhibit K); Clark (1998), *The Mammary Gland as a Bioreactor: Expression, Processing, and Production of Recombinant Proteins*, Vol. 3, No. 3 (Exhibit L); Echelard and Meade (2003), *Protein production in transgenic animals*, Chapter 24, S.C. Makrides (Ed.) *Gene Transfer and Expression in Mammalian Cells* (Exhibit M).

As the Examiner's opinions are not sufficient to establish by a preponderance of evidence that one of ordinary skill in the art would not recognize a description of mammalian milk protein promoters in the instant application, and have been contradicted with the above arguments and evidence, withdrawal of this rejection is respectfully requested.

Rejections Under 35 U.S.C. §103

The Examiner has rejected claims 1, 2, 5-8, 16, 17, 30 and 31 under 35 U.S.C. §103(a) as being unpatentable over Qasba et al. (1984, Nature, Vol. 308, pgs 377-380) and Bujard et al. (US Patent 4,495,280-Jan.22, 1985). The Examiner argues that Qsaba et al. teach the rat alpha-lactalbumin gene, and Bujard et al. teach the use of constructs to drive expression of transgenes. The Examiner then concludes that it would have been obvious to one of ordinary skill in the art at the time of the filing of the instant application to combine these teachings to obtain the claimed constructs to drive expression of a gene of interest for the commercial production of polypeptides.

Applicant respectfully traverses. Applicant maintains that the Examiner has failed to establish a *prima facie* case of obviousness. No sufficient reasoning to establish that it would have been obvious for a person of ordinary skill in the art to select the rat alpha-lactalbumin promoter to drive expression of a gene of interest has been provided. In fact, the Examiner provides no reason whatsoever why this particular promoter would be selected. According to the Supreme Court "Rejections on obviousness cannot be sustained by mere conclusory statements; instead there must be some articulated reasoning with some rational underpinning to support the

legal conclusion of obviousness” KSR Int’l v. Teleflex Inc., 82 USPQ2d 1396 (2007). Such articulated reasoning with rational underpinning to sustain this rejection has not been provided, and the Examiner has impermissibly used hindsight to reach his conclusion of obviousness.

In addition, in order to assert a *prima facie* case of obviousness, a reasonable expectation of success must be demonstrated. In re Merck & Co., Inc., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). The Examiner has failed to establish that it was reasonably expected that gene expression could be accomplished with the rat alpha-lactalbumin promoter. Without such an expectation, one of ordinary skill in the art would have no reason to select the promoter and create the constructs of the instant claims. In addition, while not required, Applicant has provided evidence that supports the notion that Applicant’s invention was truly groundbreaking. In fact, it was due to Applicant’s invention that a “mini-revolution” was started and an entire industry was founded. See Paragraph 9 of the Declaration of Harry M. Meade (previously filed with the response to the Final Office Action of May 3, 2007). Up until the 1987 publication describing the invention of the instant application, proteins encoded by foreign genes were not expressed in a medium from which they could readily be obtained and purified. See Paragraph 6 of Ibid.

Accordingly, withdrawal of this rejection is respectfully requested.

Double Patenting Rejections

The Examiner has rejected claims 1, 2, 5-8, 11, 16 and 17 on the ground of nonstatutory obviousness-type double patenting as allegedly being unpatentable over claims 1-5 of U.S. Patent No. 6,727,405. The Examiner has also rejected claims 1, 2, 5-8, 11, 16, 17 and 30-33 on the ground of nonstatutory obviousness-type double patenting as allegedly being unpatentable over claims 1-41 of U.S. Patent No. 7,045,676.

Without conceding the correctness of the rejection, and in the interest of expediting prosecution, Applicant anticipates filing terminal disclaimers to obviate this rejection. See MPEP 804.02 at page 800-32, column 1 (A terminal disclaimer “is not an admission of the propriety of the rejection”).)

CONCLUSION

A Notice of Allowance is respectfully requested. The Examiner is requested to call the undersigned at the telephone number listed below if this communication does not place the case in condition for allowance.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, the Director is hereby authorized to charge any deficiency or credit any overpayment in the fees filed, asserted to be filed or which should have been filed herewith to our Deposit Account No. 23/2825, under Docket No. G0744.70042US07.

Respectfully submitted,

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